20. (New) The method of claim 19 wherein the symptom is pulmonary edema.

21. (New) The composition of claim 18 wherein the daily dose of the cortisol antagonist to a subject being treated is 100-200 mg.--

REMARKS

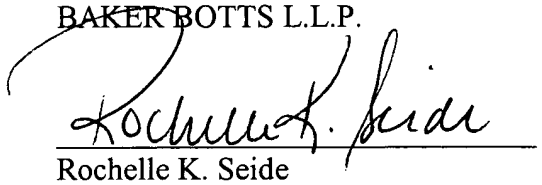
Prior to examination of the above-captioned application, Applicants respectfully request consideration of this amendment and remarks made herein. Claims 1-12 are pending. Claims 1-12 have been cancelled and Claims 13-21 have been added to more clearly state the subject matter of the invention. The specification has been amended to include cross-reference to related applications and to include an abstract of the disclosure on a separate page following the claims. No new matter has been added by the amendments made to the specification or the claims.

In accordance with 37 C.F.R. § 1.121, Applicant has provided (1) accurate instructions to amend the specification and claims, (2) a substitute specification and amended claims in clean form herein, and (3) another version of the substitute specification and amended claims marked up to show all the changes relative to the previous version of the claims.

Applicants request an early and favorable consideration of Claims 13-21.

Respectfully submitted,

BAKER BOTTS L.L.P.



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MARKED UP VERSION OF TECHNICAL AMENDMENTS

IN THE TITLE:

Please amend the title as follows:

USE OF CORTISOL ANTAGONISTS IN THE TREATMENT OF[FOR] HEART FAILURE

IN THE SPECIFICATION:

Please insert the following text before the first paragraph of the specification:

--CROSS REFERENCES TO RELATED APPLICATIONS

This application is a national stage filing of International Patent Application PCT/GB00/02551, filed 3 July 2000, which claims priority from Great Britain Patent Application 9915625.9, filed 2 July 1999.--

Please insert the following text into the specification on page 18:

--ABSTRACT OF THE DISCLOSURE

The present invention relates to the use of a cortisol antagonist in the manufacture of a medicament for the treatment of heart failure as well as to a method of treating heart failure which comprises administration of a cortisol antagonist and to a product containing (a) a cortisol antagonist and (b) a second drug as a combined preparation for simultaneous, separate or sequential use in the treatment of heart failure or in improving cardiac function and reducing exercise intolerance.--

IN THE CLAIMS:

Please cancel original Claims 1-12.

Please add the following new Claims 13-21:

--13. (New) A method for the treatment of a cardiac pathology in a mammal which comprises administering a cortisol antagonist to said mammal in an amount effective to treat the cardiac pathology.

14. (New) The method of claim 13 wherein the cardiac pathology is selected from the group consisting of congestive heart failure, diastolic heart failure, low-output heart failure, right-sided heart failure, cardiac hypertrophy, and cardiac fibrosis.

15. (New) The method of claim 14 wherein the cortisol antagonist is an inhibitor of cortisol synthesis.

16. (New) The method of claim 15 wherein the inhibitor of cortisol synthesis is ketoconazole or a derivative thereof.

17. (New) The method of claim 16 wherein the cortisol synthesis inhibitor is a Cis-2S,4R and/or Cis-2R,4S isomer of ketoconazole.

18. (New) A composition for daily administration to a mammalian subject comprising:

i) a cortisol antagonist, and

ii) a second drug,

as a combined preparation for simultaneous, separate or sequential use in the treatment of heart failure or in improving cardiac function and reducing exercise intolerance.

19. (New) A method for the treatment of one or more symptoms associated with heart failure selected from the group comprising edema of lower limbs, pulmonary edema, dyspnea,

liver enlargement, increased heart rate, reduced stroke volume, shortness of breath and exercise intolerance which comprises administering of the composition of claim 18 to a mammalian subject.

20. (New) The method of claim 19 wherein the symptom is pulmonary edema.

21. (New) The composition of claim 18 wherein the daily dose of the cortisol antagonist to a subject being treated is 100-200 mg.--